PARTICIPANT INFORMATION AND CONSENT FORM

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INTRODUCTION

You are being asked to participate in this research study. Please take time to review this consent form and discuss any questions you may have with the study staff before agreeing to participate in the described experimental research. You may discuss it with your regular doctor, friends, and/or family

before you make your final decision. This consent form may contain words that you do not understand. Please ask the Principal Investigator, Co-Investigators, or study staff to explain any words or information you do not clearly understand.

BACKGROUND OF STUDY

The prevalence of Type-2 diabetes has increased worldwide, and New Brunswick is no exception. It is understood that exercise can be an effective way to control blood glucose and prevent the progression towards Type-2 diabetes. However, research suggests there is large interindividual variation in the blood glucose response to any exercise program. This is believed to result in a number of people who do not benefit from exercise, known as non-responders. Emerging evidence proposes that altering an exercise program and providing a sufficient exercise stimulus can improve the number of people who respond to exercise, leading to a reduction in the number of non-responders. While this is encouraging, to date there have been no attempts to reduce the number of non-responders across a population of individuals living with prediabetes or Type-2 diabetes, or to observe if there are long-term health implications associated with responding (or not responding) to exercise.

This study is being conducted based on previous studies that indicated an increase in exercise intensity can lead to a higher proportion of exercise responders (In other words, more people benefiting from exercise). In addition, no research has looked at the effects of maintaining the original exercise prescription and comparing it to a higher intensity exercise prescription. We suspect that; 1) a meaningful number of participants will not improve their blood glucose following the original 16-week exercise prescription, 2) the non-responder participants who increase the intensity of the exercise prescription during the next 12-weeks will see an greater improvement in their blood glucose levels compared to the non-responders who continue with the original program, and 3) responding to the exercise program will lead to health benefits 1-year following the cessation of the exercise programs.

OBJECTIVES OF THE STUDY

The purpose of this study is to find out 1) how common non-response to a standard exercise program is amongst individuals living with prediabetes or Type-2 diabetes, 2) if increasing the intensity of the exercise program can lead to more responders than simply maintaining current exercise, and 3) if there are long-term benefits associated with responding.

WHY WERE YOU ASKED TO PARTICIPATE IN THIS STUDY?

You are being asked to take part in this study because you are above 19 years of age, currently have blood glucose levels that indicate you may be living with prediabetes or Type-2 diabetes and are not currently engaged in a structured exercise program. A total of 60 participants will be in this study.

Participation Timeline:

Week	1		2 – 17	18		19 – 31	32		84
Visit	1	2	3 – 50	51	52	53 – 88	89	90	91
Questionnaires	X		16 weeks exercise training (Approximately 3-5 visits each week totaling 150 minutes) Submaximal fitness testing every 4 weeks			12 weeks exercise training (Approximately 3 visits each week totaling 150 minutes) Submaximal fitness testing every 4 weeks			X
Height, Weight, Waist Circumference, Body Composition	X			X			X		X
Physical Activity & Dietary Assessment	X						X		X
Bloodwork	X	X		X	X		X	X	X
Fitness Test	X	X		X	X		X	X	X
Feces collection	X			X			X		

STUDY PROCEDURES
Listed below are the tests and procedures involved in participating in this study:

1. Medical History

You will be asked a series of questions regarding your health and any current mediations being taken.

2. Physical Activity, Dietary Recall, Screen Time and Sedentary Behaviour, Self-Regulation Eating and Addiction Questionnaires

You will be asked to complete a series of questionnaires outlining your current level of physical activity and sedentary behaviour, the total amount of screen time you engage in, and your dietary habits. In addition, questionnaires about your self-regulation and potential eating addiction will be completed.

3. Gender Role and Mental Health Questionnaires

You will be asked to fill out questionnaires meant to help us adequately understand your perceived gender role and understand your current mental health status.

4. Body Measurements

We will measure your body weight, height, and take a measurement of your waist circumference.

5. Body Composition

We will look at the amount of muscle and fat in your body using a Bod Pod. In order to do that, you will be asked to wear a bathing suit and swim cap while sitting in a device called the Bod Pod. The Bod Pod resembles an egg-shaped chamber with a window for you to look out of. Air will move into the enclosed space where you sit and you may feel a slight change in air pressure. While enclosed in this chamber, if you begin to feel uncomfortable, you can press a button located by your knee to open the door. The Bod Pod measures the airflow and the changes in the airflow that occur while your body is in the chamber. You are to sit quietly while the first measurements of airflow are conducted. This takes about 30 seconds, at which time the technician will open and close the Bod Pod door to repeat the measurement again. The whole test takes approximately 5 minutes. The test is performed in a private room. To accurately complete this test, it is required that you do not eat or drink any beverage for at least 4 hours, or smoke for at least 2 hours before the test starts.

6. Blood Work at UNB

A registered nurse will take a draw of your blood (equating to approximately 6 tablespoons) for our analysis purposes. Specifically, we will analyze the concentrations of glucose, insulin, and a protein named irisin, present in your blood. To complete this test, it is required that you fast overnight.

7. Fitness Test

At the CELLAB we will measure your heart and lung fitness levels. This test takes approximately 8 to 12 minutes. The exercise test will be performed on a treadmill. We will measure your heart rate and blood pressure during the test. Heart rate will be measured with a small black band around your chest, and blood pressure is measured with a cuff on your arm. We will also measure your breathing during the exercise test. To do this, you will be required to wear a mouth piece or mask to properly throughout the test. To start, you will be asked to walk at an easy pace with no incline. We will then progressively increase the slope 1% every minute. You will decide when to stop the test; the study staff will encourage you to continue as long as you can. To accurately complete this test, it is required that you do not consume caffeine, eat, or smoke within 3 hours, or exercise within 12 hours of the test.

8. Physical Activity and Dietary Assessment

You will leave the CELLAB with a pedometer to wear for seven days following the first visit. The pedometer is a small device that you will be asked to wear on your left hip to track your daily physical activity levels. This device must be returned upon completion. You will also receive physical activity log to fill out for one week, asking you to take record of how may steps you took each day, alongside any additional physical

activity you complete. Finally, you will receive a dietary log to be completed every day for one week. On this log you will need to record any food and/or beverage you consume every day for one week.

9. Exercise Training

Following visit 1 and 2, you will be randomized into one of two groups. The first group will not be provided any exercise intervention to complete from week 2 to 17, or from week 19 to 31. However, various prizes will be awarded to those participants who successfully show up to all testing sessions (week 1, week 18, week 32). Once this group has completed the final testing, they will be offered to opportunity to partake in the exercise offered to the second group.

The second group will be prescribed moderate intensity aerobic exercise from weeks 2 to 17. During the first week of exercise, you will be required to complete 80 minutes of moderate intensity aerobic exercise. The duration of exercise will slightly increase in each subsequent week for the first four weeks of exercise training (week 2 – 5). From week 6 – 17 you will complete 150 minutes of moderate intensity aerobic exercise per week. The CELLAB will be open at various times throughout the week, providing you with ample opportunity to complete the required exercise. Optimally, participants will come three times per week, with each session consisting of 50 minutes of exercise. The minimum number of sessions that can be used to complete the 150 minutes of exercise is **two**. Every four weeks you will complete a submaximal treadmill walking test (as described below) to allow the study group to adjust the intensity of your training to your potentially improved fitness level.

After testing visits 51 and 52 (during week 18), participants in the second group will be randomized into two exercise programs. **You will not be informed if you are a responder or a non-responder until the study is completed.** Participants in the first exercise program will continue their current exercise prescription for 12 weeks (week 19 – 31). Participants randomized to the second exercise program will still complete 150 minutes of exercise per week, however they will do so at a slightly higher intensity (moderate to vigorous). Submaximal treadmill walking tests will again be completed every four weeks to allow the study group to adjust exercise Intensity as necessary.

10. Submaximal Fitness Tests

Every four weeks throughout the exercise training you will complete a submaximal treadmill walking test. We will measure your heart rate and your breathing during the test. Heart rate will be measured with a small black band around your chest. Measuring your breathing will required to wear a mouth piece or mask while walking on the treadmill for 4 minutes at a pre-determined grade and speed.

11. Feces collection

You will be asked to provide a fecal sample at baseline, after the initial 16 weeks of exercise and at post-testing. Therefore, a total of 3 time-points will be recorded. Although this type of measurement is usually unpleasant, we have taken every means available to make this as easy as possible for you. A fecal sample collection kit will be provided by our research team. The research staff will provide you with detailed instructions as well as an instructional online video. The fecal sample will be collected by you, in your

home, and then brought back to the lab within 2 days. The sample will be stored appropriately in a -80°C freezer. This procedure does not have any risk associated with It, other than the potential discomfort associated with the collection (which will happen in the comfort of your home). The collection of fecal samples will provide further insight into exercise responders vs. non-responders (using glycemic control), following an exercise intervention.

STUDY VISITS

Visit 1 & 2 (within 1 week of each other)
Location: UNB CELLAB

- Review and sign the Informed Consent (Visit 1 only)
- Medical History (Visit 1 only)
- Questionnaires (Visit 1 only)
- Weight, height, hip, and waist measurement
- Body Composition
- Bloodwork
- Fitness Test
- Physical Activity & Dietary Assessment & Questionnaires

Each visit takes about 2 hours

Visits 3 – 50 (Group 2 participants only)
Location: UNB CELLAB Gym

- Exercise Training
- Submaximal Treadmill Walking Test (Every 4 weeks)

Visit 51 & 52 (within 1 week of each other)
Location: UNB CELLAB

- Weight, height, hip, and waist measurement
- Body Composition
- Bloodwork
- Fitness Test

Each visit takes about 2 hours

Visits 53 – 88 (Group 2 participants only)
Location: UNB CELLAB Gym

- Exercise Training
- Submaximal Treadmill Walking Test (Every 4 weeks)

Visit 89 & 90 (within 1 week of each other)

Location: UNB CELLAB

- Weight, height, hip, and waist measurement
- Body Composition
- Bloodwork
- Fitness Test
- Physical Activity & Dietary Assessment & Questionnaires
  Each visit takes about 2 hours

Visit 91 (One year later)
Location: UNB CELLAB

- Medical History (Visit 1 only)
- Questionnaires (Visit 1 only)
- Weight, height, hip, and waist measurement
- Body Composition
- Bloodwork
- Fitness Test
- Physical Activity & Dietary Assessment & Questionnaires
  Each visit takes about 2 hours

POTENTIAL RISKS AND DISCOMFORT

Study personnel are trained to respond to any emergency and a registered nurse and will be on site during the necessary procedures.

Physical Activity and Dietary Assessment: There are no risks associated with wearing a pedometer. It is possible that the pedometer makes you feel uncomfortable, but that is unlikely.

Body Composition: During the Bod Pod testing, it is possible that you might experience some light-headedness or dizziness. It is also possible that if you are claustrophobic, that you may begin to have a feeling of being shut-in. A button at your knee while you are inside of the Bod Pod, will allow you to have the door of the Bod Pod open *immediately*. A window on the Bod Pod also will allow you and the technician to see and communicate with one another. There is no physical danger involved in these measurements. Room air is continuously circulated through the Bod Pod compartment when it is closed. The compartment does not lock and the person inside can exit at any time. Your parent/legal guardian will be present at all time during this test with someone from our research staff. The test is performed behind a medical curtain to maintain privacy and ensure nobody see you.

Exercise Training: When people exercise for the first time in a long while, there is the possibility of an increased risk of muscle or joint injuries. However, all exercise will be performed in the presence of a trainer who will know exactly what to do in case a physical injury, or any additional concern, occurs. Also, the selected training methods, duration, and Intensity in this program were carefully chosen to minimize injury risk and optimize the benefits for each participant. The research staff is educated in proper exercise prescription for individuals living with diabetes, and will follow the 2018 Diabetes Canada Guidelines for exercise in order to ensure each participant is properly monitored, prepared, and advised as recommended throughout the exercise training program. It is possible that the heart rate monitor worn throughout each session will make you feel uncomfortable, but we have a variety of models that may be used, and discomfort is unlikely.

Bloodwork: Some people experience slight discomfort, bleeding and/or bruising during the collection of blood samples. Sometimes people feel dizzy or faint. An infection in your arm can develop if the testing site is not clean, so the nurse will clean your arm with alcohol before taking blood. Every effort will be made to reduce any risks and discomfort. We have a registered nurse that will do all the blood collection.

Fitness Tests: There is a possibility of certain changes occurring during the exercise test. Serious complications of exercise testing occur in approximately 1 in 10,000 tests in adults. Such complications may include abnormal blood pressure, fainting, heart rate disorder and, in rare instances, heart attack, stroke and death. Exercise testing may also cause slight injury to muscles and joints, routine discomforts that will go away within three days after the test. Every effort will be made to minimize these risks by reviewing information about your health and fitness before the test and by closely monitoring how your body responds to the exercise. We will reduce these risks by closely monitoring your condition throughout the exercise test. If you experience any abnormal response to the exercise, the session will be stopped.

What Are the Potential Benefits of the Study?

Benefit to you: By participating in the study, you will receive information about your health and physical activity level. In addition, you will be provided with a personal trainer and regular access to a fitness facility at no cost to you, which would not be possible during a regular doctor's visit. It is very likely that engaging in this study will improve your health. Participants will likely learn what kind of exercise they can do to continue obtaining health benefits once the project is complete, and better understand why they are getting healthier.

Benefit to other people: The main benefit of participating in this study is the knowledge we will gain about how the body responds to exercise, and if it is possible to improve the number of responders among individuals living with prediabetes or Type-2 diabetes.

What Are the Costs of the Study?

There are no costs to you for participating in this study. This study will cover all costs, which include clinic and professional fees, along with the diagnostic and laboratory tests. A parking pass will be provided so you do not have to pay for parking.

Is the Study Confidential?

Information gathered in this research study may be published or presented in public forums, however your name and other identifying information will not be used or revealed. Medical records that contain your identity will be treated as confidential. Despite efforts to keep your personal information confidential, absolute confidentiality cannot be guaranteed. Your personal information may be disclosed if required by law.

The Research Ethics Board at the University of New Brunswick may also review your research-related records for quality assurance purposes.

Only your consent form will have information that relates to your identification number (ID) number and this will be kept in a locked cabinet within a locked room located at the University of New Brunswick. All other study documents related to you will bear only your assigned ID number. These records will be kept in a locked secure area and only those identified will have access to those records. No information revealing any personal information, such as your name, phone number or address, will leave the University of New Brunswick. All data collected will be entered into computers, however all data will be password protected and data files will not include any identifying information, only the subject ID number. All your data will be kept for 7 years and then will be destroyed.

Do I Have the Right to Change My Mind?

Your decision to take part in this study is totally up to you. You may refuse to participate or you may quit at any time. Your decision to participate or withdraw from the study will not affect your regular medical care. The investigators reserve the right to end your participation in the study for any reason.

If you are enrolled and subsequently withdraws from the study, any information or biological samples supplied up to that point remains in the possession of the research team and will be retained as data for research purposes.

What Else Should I Know?

- Any results from this study cannot be used for diagnosis.

- You may request a copy of any images and the blood tests.
- At your request, a summary of the test results can be provided to your primary care physician.
- Your primary care physician will not know whether you have agreed to participate in this study or not unless you request that a summary of the test results be provided to him or her. You may request that the test results be provided to your physician at the end of the study.
- The investigators have no financial interest in the outcome of the study.
- All the blood samples will be kept for a maximum of 7 years in a locked freezer in our exercise physiology lab, which is a restricted access room. The samples will be kept anonymous; no linkage or genetic tests are anticipated with these samples. They will be destroyed safely according to standard biohazard procedures.

If, in the opinion of the researchers, it is believed that you need further medical follow-up based on standard results you will be advised of this.

This project has been reviewed by the UNB Research Ethics Board and is on file as REB 2018-168

Potential Changes to Study Protocols due to COVID 19

Given the potential for the current COVID-19 pandemic to close University of New Brunswick facilities, or restrict face to face data collection, the study protocol will need to change. Below we outline two scenarios.

Scenario 1: Intervention not possible in CELLAB

Should face to face data collection be approved, but the University of New Brunswick restrict access to on campus facilities, exercise will instead take place at a location of your choice such as your home or a public space. The study timeline, purpose and objectives, and randomization will remain unchanged.

You will still be required to complete the weekly time allotment at the prescribed exercise intensity. Likewise, you will be able to select the time and number of sessions completed each week. However, you will be asked to place the heart rate monitor on yourself. Moreover, you will be asked to use provided steps (or a staircase in your home) and while under supervision by a research staff member via video calling software, complete the training session. You will be asked to report your heart rate every 5 minutes, and the research staff will inform you when you need to increase the intensity.

Scenario 2: Intervention and testing not possible in CELLAB

In addition to perform the exercise in at a location of your choice, the testing will be limited as well. If allow by Public Health and accepted by you, a research assistant will come into your home and performed testing to respect the study timelines.

4. Body measurements

Height and weight will be taken with portable equipment

5. Body Composition

The BODPOD will no longer be used to estimate body composition. In its place, a handheld Omron HBF-306C bioelectrical impedance analyzer will be temporarily provided. Prior to the test, you will be asked to avoid consuming any food or liquids for 4 hours prior to the test, and to use the bathroom within 30 minutes of the analysis. You will then stand straight up, and hold the monitor with your arms fully extended. The device will then complete its measurement, taking approximately 30 seconds.

6. Blood Work at UNB

All tests completed using a blood draw will be dropped from the study besides HbA1c, that will be collected through a finger prick. You will be provided instructions as to how to safely conduct a finger prick, in line with the procedures followed for daily glucose measurements. You will be provided with a small collection tube, which will be used to collect 1 µL of blood from the finger prick. The collection tube will then be taken by the research staff to conduct the analysis, and all materials disposed of in line with proper biohazard and sharps waste disposal procedures.

7. Fitness Test

In place of the maximal fitness test, a predicted aerobic fitness test will be completed. Specifically, the modified Canadian Aerobic Fitness Test (mCAFT) will be used. You will be provided with a heart rate monitor, the mCAFT music, and sanitized, standardized set of steps. You will also be provided the link to a video showing how to properly put on a heart rate monitor, and how to make sure it is working, as well as clear instructions on how to complete the test. While supervised by a research staff member over an online video chatting software, you will listen to the music and follow the audio cues to step up and down the provided steps at the required cadence, completing 3-minute stages until cut off by the research staff member. You will be asked to report their heart rate between each stage. A predictive equation will then be used to estimate the participant's maximal aerobic fitness.

10. Submaximal Fitness Test

Instead of completing the submaximal treadmill walking tests, every four weeks you will be asked to repeat the mCAFT test, as outlined previously.

How Can I Get More Information?

To receive additional **information** about this study from the researchers:

- Martin Sénéchal, Ph.D., CEP (506) 451-6889

For questions about your **rights as a research subject**, you may contact:

- Wayne Albert, Dean of the Faculty of Kinesiology (506) 453-4575
- Steven R. Turner Chair of UNB Research Ethic Board (506) 458-7433

Signatures

- I have received a copy of this consent form and I have read it. I understand the nature of the study, including the potential risks and benefits. I have had adequate time to consider the information. My questions about the study have been answered.
- I will be given a copy of this document, after signing it.
- By signing this document, I am not waiving any of my legal rights and I understand that I can stop being in the study at any time.
- **I hereby agree to participate in the study outlined throughout this document.** My consent has been given freely.
- I wish to be contacted for future studies. (Additional consent will be required and I will be free to decline participation in any further studies at the time of contact.)

  YES ❑ **NO** ❑

I wish to receive a report of the results of this study when available. ❑

Consent of the Participant (Print)	Signature	Date

Person Obtaining Consent

To the best of my knowledge, the information that I have provided in response to any questions fairly represents the project. I am committed to conducting this study in compliance with all the ethical standards that apply to projects that involve human subjects.

Name (Print)	Signature	Date